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Printed by Min Chen

Electronic Mail Message

Sensitivity: COMPANY CONFIDENTIAL

Date: 05-Oct-1999 10:10am
From: Charles Ganley
GANLEY
Dept: HFD-560 CRP2 S205
Tel No: 301-827-2241 FAX 301-827-2316

TO: Min Chen (CHENMI)

CC: Peter Honig (HONIGP)
CC: Charles Ganley (GANLEY)
CC: Debra Bowen (BOWEND)
Subject: Re: preliminary review of ephedra/ephedrine materials from CFSAN

Min,

Thanks for the quick turnaround. I just need to clarify some things for myself.

1) There are 96 reports for ephedrine in the entire database when used for asthma. Four of these are deaths. There are 122 reports for ephedrine when used as a stimulant, weight loss, misc. Twenty-five of these are deaths. Is this correct? Does the latter group only include ephedrine and not phenylpropanolamine? When were the majority of these cases in the latter group reported? Are they pre-1997? We need to discuss this.

2) In your comment #2, can you explain this a little further. You note that the ephedra ADRs were related to CVA or CV in a young population. "These were similar to the ephedrine misuse group." How do define the misuse group? By indication? By amount ingested?

3) Your comment "These products should be safe if used correctly, therefore, the issues may be how to enforce the use and dosage instructions, warnings for unsafe use and dosage, etc." I don't necessary agree because there is limited regulatory control over these products now. Thus, we have to look at these products based on what we can and can not do. As long as they can combine ephedra with an unlimited number of other ingredients (e.g. other sympathomimetics) and encourage use for indications that may not be safe for even generally healthy users, there is always going to be a problem.

4) Are there other databases that we need to look at e.g. poison control centers.

If we can meet sometime this week to discuss, I would appreciate it. I will be in Parklawn for another meeting on Thursday at 3 pm.

charley

>Hi, Charley,
>
>As discussed, here is a brief summary of what I had found.
>
>1. Dr. Woosley's review was based on 140 reports but did not provide
>what the year period covered in these reports and no Table was provided
>for any details of the analysis. For example, he mentioned 7 reports of
>cardiac arrest or sudden death, but it was unknown if it represented
>total counts of deaths from this subset or there were other deaths from
other categories, no dosage issue was discussed, or any mention of
other
>ingredients contributing to the reported events.
>
>2. Dr. Love's review and anaylses were very extensive based on 139

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The Chemins Company, Inc.
1825-35 East Cheyenne Road, P.O. Box 2498, Colorado Springs, Colorado 80906-2498 (719) 579-9650

November 3, 1999

Dirk Aschmoneit
Metabolife International, Inc.

Dear Dirk,

I have confirmed that USP caffeine is currently being used in our Guarana (seed) 20% caffeine product. Regarding your request for natural caffeine to be added to Guarana to achieve 20% caffeine levels, it can be done but there are a few issues to consider:

1. The source of natural caffeine comes from coffee beans in South America. Coca Cola is the largest buyer of natural caffeine which can create supply issues. Our current suppliers feel there is enough supply of natural caffeine to accommodate our needs at this time.

2. The cost of natural caffeine is approximately $6.00 per kilo higher than USP caffeine. This increase would adjust your bottle cost to $3.71 from $3.56.

3. Lead time to make this change for finished product is approximately 6 weeks - 4 weeks to receive the new Guarana 20% and 2 weeks to produce finished product containing the new ingredient.

Please let me know your thoughts.

Sincerely,

The Chemins Company, Inc.

Dave Humann
Vice President

efax# 815-377-9331